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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,730	01/05/2007	Robert A. Burne	5853-454-1	5558
30448	7590	05/26/2009	EXAMINER	
AKERMAN SENTERFITT			TONGUE, LAKIA J	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,730	BURNE ET AL.	
	Examiner	Art Unit	
	LAKIA J. TONGUE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 11 April 2009.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-59 is/are pending in the application.
 4a) Of the above claim(s) 14-17,24-27 and 53-59 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-8,10-12,18-23,28-38 and 44-52 is/are rejected.
 7) Claim(s) 9,13 and 39-43 is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 06 April 2006 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/9/08 and 4/6/06</u> . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, claims 1-13, 18-23 and 28-52, in the reply filed on April 11, 2009 is acknowledged.

Consequently, claims 1-59 are pending. Claims 14-17, 24-27 and 53-59 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-13, 18-23, 28-52 are currently under examination.

Information Disclosure Statement

2. The information disclosure statements (IDS) submitted on July 9, 2008 and April 6, 2006 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see pages 20, 24 and 56). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

4. Claims 9, 13 and 38-43 are objected to for depending on a rejected based claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 28-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 28-33 are drawn to a recombinant bacterial cell comprising an isolated nucleic acid construct, said cell expressing at least one alkalinizing enzyme, wherein said nucleic acid construct comprises a pMJB8 vector, a pMC321 vector, a pMC340A, a pMC340B vector, a pMC341A vector or a pMC341B vector.

Because it is not clear that the properties of plasmids **pMJB8, pMC321, pMC340A, pMC340B, pMC341A** and **pMC341B** are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of a suitable deposit for patent purposes a deposit in a public repository is required. Without a publicly available deposit of the above plasmids **pMJB8, pMC321, pMC340A, pMC340B, pMC341A** and **pMC341B**, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed.

The specification does not provide a referral to a deposit of plasmids **pMJB8, pMC321, pMC340A, pMC340B, pMC341A** and **pMC341B**, consequently the specification is an insufficient assurance that all required deposits have been made and

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all the conditions of 37 CFR 1.801-1.809 have been met. If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by the International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application. These requirements are necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring: (a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request; (b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application; (c) the deposits will be maintained in the public repository for a period of at least thirty years from the date of deposit or for

the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and (d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the repository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of biological material not made under the Budapest Treaty must be filed in the application and must contain: 1) The name and address of the depository; 2) The name and address of the depositor; 3) The date of deposit; 4) The identity of the deposit and the accession number given by the depository; 5) The date of the viability test; 6) The procedures used to obtain a sample if test is not done by the depository; and 7) A statement that the deposit is capable of reproduction. As well as a statement that removes restrictions to provide access to this strain upon granting of a patent has not made, either in the instant Specification, nor in Applicant's Remarks.

One of the critical conditions of Deposit is defined in 37 CFR 1.808 requires that the deposit of biological material be made under two conditions: (A) access to the deposit will be available during pendency of the patent application making reference to the deposit to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 U.S.C. 122, and (B) with one exception, that all restrictions imposed by the depositor on the availability to the public of the deposited biological

material be irrevocably removed upon the granting of the patent. Upon making this statement, the rejection under 35 USC 112, first paragraph will be withdrawn. This rejection can be obviated through perfection of the Deposit and amendment of the claims to clearly set forth the Deposited strains.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit. If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the plasmids **pMJB8, pMC321, pMC340A, pMC340B, pMC341A and pMC341B** described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed. Applicant's attention is directed to In re Lundack, 773 F.2d.1216, 227 USPQ (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5, 7, 8, 10, 12, 18-21, 23, 34-38 and 44-52 are rejected under 35

U.S.C. 102(b) as being anticipated by Clancy et al. (*Infection and Immunity*, 2000;

68(5): 2621-2629).

The rejected claims are drawn to a recombinant bacterial cell comprising an isolated nucleic acid construct, said cell expressing at least one alkalinizing enzyme.

Clancy et al. disclose the use of urease enzymes of oral bacteria to hydrolyze urea to ammonia, which can neutralize plaque acids. Clancy et al. disclose that recombinant, ureolytic strains of *Streptococcus mutans* were constructed. Specifically, the ureABCEFGD operon from *Streptococcus salivarius* 57.I was integrated into the *S. mutans* chromosome in such a way that the operon was transcribed from a weak, cognate promoter in *S. mutans* ACUS4 or a stronger promoter in *S. mutans* ACUS6. Clancy et al. disclose that both strains expressed NiCl₂-dependent urease activity. Moreover, Clancy et al. disclose that the integration of the antibiotic resistance and urease genes into the *S. mutans* chromosome was confirmed by Southern blotting (see page 2622-DNA manipulations). Clancy et al. disclose that the urease genes were cloned as a cassette into the *S. mutans* lac sequences on the integration vector with concomitant replacement of the tetracycline resistance gene (see page 2622). Clancy et al. disclose that recombinant strains confirmed that integration of the *ure* genes and selective markers occurred in the *lac* locus (see page 2623). Clancy et al. disclose that when no additional NiCl₂ was added to the medium the strains expressed urease (see page 2624). Clancy et al. disclose that recombinant strains produce functional urease

in the absence of exogenous nickel *in vitro* and *in vivo* (see page 2627-discussion). Clancy et al. disclose that the use of alkali-generating bacteria should be considered for replacement therapy (see page 2628). Clancy et al. disclose that subjects were infected with the recombinant strain and fed a cariogenic diet with drinking water containing 25 mM urea and 50 µM NiCl₂ had relatively high levels of oral urease activity, as well as dramatic decreases in the prevalence of smooth-surface caries and the severity of sulcal caries, relative to controls, indicating that ureolytic bacteria may be useful to promote dental health (see abstract).

The instantly claimed invention is identical to that of the prior art. Absent evidence to the contrary, the recombinant bacteria of Clancy et al. necessarily produces an agmatine deiminase enzyme, the vector is necessarily stably integrated into the genome, the vector necessarily targets a *mtl* gene and the *ureABCEFGD* necessarily comprises a nickel transporter.

7. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (*Infection and Immunity*, 1996; 64(2): 585-592).

The rejected claims are drawn to a recombinant bacterial cell comprising an isolated nucleic acid construct, said cell expressing at least one alkalinizing enzyme.

Chen et al. disclose a study of the urease of *Streptococcus salivarius*, a highly ureolytic organism. Chen et al. disclose that an internal fragment of the *S. salivarius* 57.I *ureC* gene, two clones from subgenomic libraries of *S. salivarius* 57.I in an *Escherichia coli* plasmid vector were identified. Chen et al. disclose that nucleotide

sequence analysis revealed the presence of one partial and six complete open reading frames which were most homologous to ureIAB-CEFGD of other ureolytic bacteria.

Plasmid clones were generated to construct a complete gene cluster and used to transform *E. coli* and *Streptococcus gordonii* DL1. Moreover, Chen et al. disclose that the recombinant organisms expressed high levels of urease activity when the growth medium was supplemented with NiCl₂ (see abstract).

8. Claims 1-6, 10, 11, 18, 19, 21, 38 and 52 are rejected under 35 U.S.C. 102(a) as being anticipated by Dong et al. (*Applied and Environmental Microbiology*, 2002; 68(11): 5549-5553).

The rejected claims are drawn to a recombinant bacterial cell comprising an isolated nucleic acid construct, said cell expressing at least one alkalinizing enzyme.

Dong et al. disclose that an arginine deiminase (AD) system (ADS) is one of two major ammonia-generating pathways in the oral cavity that play important roles in oral biofilm pH homeostasis and oral biofilm ecology. Dong et al. disclose that *Streptococcus gordonii* ADS and the ADS gene cluster were isolated from subgenomic DNA libraries of *S. gordonii* DL1 by using an *arcB*-specific probe (see abstract). Dong et al. disclose genes encoding enzymes for arginine in *S. gordonii*. Dong et al. disclose genetically engineered, ammonia-producing oral streptococci as potential agents for the control of dental caries expressing the urease genes of *Streptococcus salivarius* in *Streptococcus mutans* (see page 5552). Dong et al. disclose the similarities between the deduced amino acids sequences of *arcABCDTR* of *S. gordonii* (see page 5551). Moreover,

Dong et al. disclose that conserved amino acid residues for arginine binding were found in *S. gordonii* (see page 5551).

The instantly claimed invention is identical to that of the prior art. Absent evidence to the contrary, the vector of Dong et al. necessarily targets a *mtl* gene.

Since the Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the prior art.

See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dong et al. (*Applied and Environmental Microbiology*, 2002; 68(11): 5549-5553) as applied to claims 1-6, 10, 11, 18, 19, 21 and 52 above.

The rejected claims are drawn to a recombinant bacterial cell comprising an isolated nucleic acid construct, said cell expressing at least one alkalinizing enzyme. Dong et al. disclose that an arginine deiminase (AD) system (ADS) is one of two major ammonia-generating pathways in the oral cavity that play important roles in oral biofilm

pH homeostasis and oral biofilm ecology. Dong et al. disclose that *Streptococcus gordonii* ADS and the ADS gene cluster were isolated from subgenomic DNA libraries of *S. gordonii* DL1 by using an *arcB*-specific probe (see abstract). Dong et al. disclose genes encoding enzymes for arginine in *S. gordonii*. Dong et al. disclose genetically engineered, ammonia-producing oral streptococci as potential agents for the control of dental caries expressing the urease genes of *Streptococcus salivarius* in *Streptococcus mutans* (see page 5552). Dong et al. disclose the similarities between the deduced amino acids sequences of *arcABCDTR* of *S. gordonii* (see page 5551). Moreover, Dong et al. disclose that conserved amino acid residues for arginine binding were found in *S. gordonii* (see page 5551).

Dong et al. do not specifically disclose that the carrier is selected from the group consisting of a chewing gum, toothpaste, a lozenge, a powder, a gel, an ointment, a cream, a liquid, a mouthwash, a rinse and a candy.

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Dong et al. to include said recombinant bacterial cell with a carrier selected from the group consisting of a chewing gum, toothpaste, a lozenge, a powder, a gel, an ointment, a cream, a liquid, a mouthwash, a rinse and a candy because Dong et al. disclose that the study provides the foundation for exploiting the use of arginine catabolism to moderate plaque acidification and to control the emergence of a cariogenic flora see pages 5552-3) and Clancy disclose that ureolytic bacteria maybe useful to promote dental health (see abstract). Moreover, the claim would have been obvious because the design incentives or market forces provided a

reason to make an adaptation, and the invention resulted from application of the prior knowledge in a predictable manner (see the recent Board decision *Ex parte Smith*,-- *USPQ2d*--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 *USPQ2d* at 1396). One would have had a reasonable expectation, barring evidence to the contrary, that the composition would be effective.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

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LJT
5/22/09

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645